(FILE 'HOME' ENTERED AT 19:58:45 ON 26 MAY 2006)

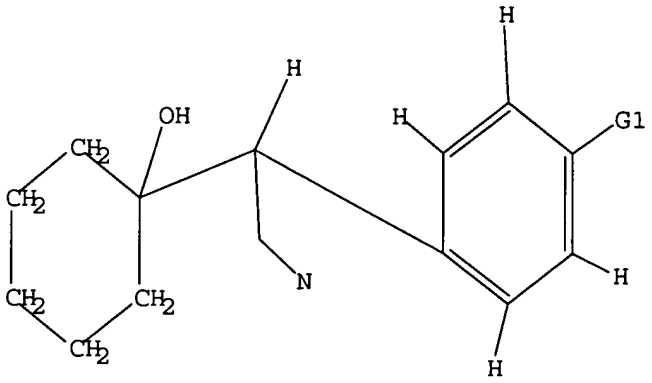
FILE 'REGISTRY' ENTERED AT 19:58:56 ON 26 MAY 2006
L1 STRUCTURE UPLOADED
L2 7 S L1
L3 104 S L1 FUL

FILE 'CAPLUS, CAOLD' ENTERED AT 19:59:49 ON 26 MAY 2006
L4 11 S L2
L5 1151 S L3

FILE 'REGISTRY' ENTERED AT 20:00:29 ON 26 MAY 2006
L6 4 S E CYCLOHEXANONE
L7 1 S CYCLOHEXANONE/CN
L8 4 S L6
E CYCLOHEXANONE
L9 30063 S E3

FILE 'CAPLUS, CAOLD' ENTERED AT 20:02:06 ON 26 MAY 2006
L10 26323 S L7
L11 6 S L4 AND L10
L12 3 S L11 AND ?HYDRIDE?
L13 3 S L11 NOT L12
L14 1140 S L5 NOT L4
L15 21 S L14 AND L10
L16 2 S L15 AND ?HYDRIDE?
L17 19 S L15 NOT L16

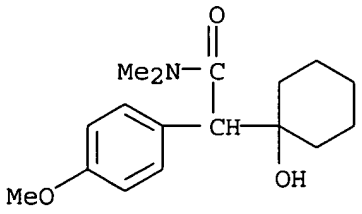
=> d l1
L1 HAS NO ANSWERS
L1 STR



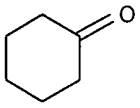
G1 OH,MeO,EtO,n-PrO

Structure attributes must be viewed using STN Express query preparation.

L12 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:263216 CAPLUS
DN 144:90006
TI An improved novel method for venlafaxine synthesis
AU Sheng, Rong; Liu, Tao; Hu, Yongzhou
CS College of Pharmaceutical Sciences, Zhejiang University, Hangzhou, Zhejiang Province, 310031, Peop. Rep. China
SO Zhejiang Daxue Xuebao, Yixueban (2004), 33(1), 77-79
CODEN: ZDXYA9; ISSN: 1008-9292
PB Zhejiang Daxue Chubanshe
DT Journal
LA Chinese
AB Venlafaxine was synthesized with p-methoxyphenylacetic acid as the initial material. The material p-methoxyphenylacetic acid was reacted with SOCl2, to produce acyl chloride, which was reacted with N,N-dimethylamine solution to get amide. Then through Ivanov reaction and reduction by KBH4/BF3·Et2O to obtain venlafaxine. Venlafaxine was successfully synthesized by this method with the yield rate of 50.3%. The improved method is suitable for industrial production of venlafaxine.
IT **295366-48-2P**
RL: BMF (Bioindustrial manufacture); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; improved method for venlafaxine synthesis)
RN 295366-48-2 CAPLUS
CN Benzeneacetamide, α-(1-hydroxycyclohexyl)-4-methoxy-N,N-dimethyl- (9CI) (CA INDEX NAME)



IT **108-94-1**, Cyclohexanone, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; improved method for venlafaxine synthesis)
RN 108-94-1 CAPLUS
CN Cyclohexanone (7CI, 8CI, 9CI) (CA INDEX NAME)



L12 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:720419 CAPLUS
DN 133:252074
TI Process for preparing 1-[2-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol hydrochloride
IN Cheng, Guohou; Zhuo, Zhao; Zhang, Weiwei; Tang, Haixia
PA Huadong Science and Engineering Univ., Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1240206	A	20000105	CN 1999-113785	19990617
PRAI CN 1999-113785		19990617		

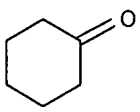
OS CASREACT 133:252074

AB The process comprises chlorinating 4-methoxyphenylacetic acid with SOCl2 by refluxing for 2-6 h, removing excess SOCl2; acylating 40% dimethylamine solution in solvent (S) to obtain N,N- dimethyl-4-methoxyphenylacetamide (A); adding isopropylmagnesium bromide in solvent (S1) at 10-30° for 4-8 h, adding with cyclohexanone at 40-45° for 5-12 h to obtain N,N-dimethyl-α-(1- hydroxycyclohexyl)-4-methoxyphenylacetamide (B); reducing with KBH4 in solvent (S1) in the presence of AlCl3 at 10-30° for 2-4 h to obtain 1-[2-dimethylamino-1-(4-methoxyphenyl)ethyl]cyclohexanol; in solvent (S2) bubbling gaseous HCl at 25-30° to pH 1-2, and crystallizing at 5-10°. The solvent (S) is benzene, chloroform, or cyclohexane; the solvent (S1) is THF, glycol di-Me ether, or Et ether; and the solvent (S2) is isopropanol, ethanol, or methanol. The mole ratio of 4-methoxyphenylacetic acid-SOCl2-dimethylamine is 1:1.2-1.4:2-4, that of compound (A)-isopropylmagnesium bromide-cyclohexanone is 1:2-3:2-3, and that of compound (B)-KBH4-AlCl3 is 1:5-7:10-12.

IT **108-94-1**, Cyclohexanone, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparing 1-[2-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol hydrochloride)

RN 108-94-1 CAPLUS

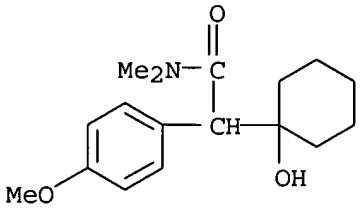
CN Cyclohexanone (7CI, 8CI, 9CI) (CA INDEX NAME)



IT **295366-48-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparing 1-[2-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol hydrochloride)

RN 295366-48-2 CAPLUS

CN Benzeneacetamide, α-(1-hydroxycyclohexyl)-4-methoxy-N,N-dimethyl- (9CI) (CA INDEX NAME)



L12 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1985:5895 CAPLUS

DN 102:5895

TI Phenethylamine derivatives and intermediates

IN Husbands, George Edward Morris; Yardley, John Patrick; Muth, Eric Anthony

PA American Home Products Corp., USA

SO Eur. Pat. Appl., 58 pp.
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

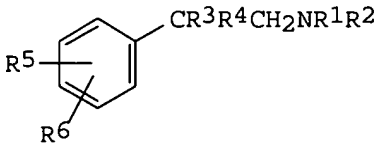
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 112669	A2	19840704	EP 1983-307435	19831207
	EP 112669	A3	19841128		
	EP 112669	B1	19870729		

R: AT, BE, CH, DE, FR, IT, LI, LU, NL, SE

	US 4535186	A	19850813	US 1983-545701	19831026
	CA 1248540	A1	19890110	CA 1983-441289	19831116
	AU 8322123	A1	19840621	AU 1983-22123	19831206
	AU 567524	B2	19871126		
	ZA 8309073	A	19840926	ZA 1983-9073	19831206
	IL 70390	A1	19861231	IL 1983-70390	19831206
	GB 2133788	A1	19840801	GB 1983-32598	19831207
	GB 2133788	B2	19870715		
	AT 28628	E	19870815	AT 1983-307435	19831207
	FI 8304523	A	19840614	FI 1983-4523	19831209
	FI 77647	B	19881230		
	FI 77647	C	19890410		
	DK 8305713	A	19840614	DK 1983-5713	19831212
	DK 166372	B	19930419		
	DK 166372	C	19930906		
	HU 33097	O	19841029	HU 1983-4231	19831212
	HU 199104	B	19900129		
	ES 527938	A1	19870101	ES 1983-527938	19831212
	JP 59116252	A2	19840705	JP 1983-235979	19831213
	JP 04012260	B4	19920304		
	US 4611078	A	19860909	US 1985-736747	19850522
	US 4761501	A	19880802	US 1985-736744	19850522
	ES 544402	A1	19880401	ES 1985-544402	19850531
	GB 2173787	A1	19861022	GB 1986-3901	19860217
	GB 2173787	B2	19870715		
	JP 03135948	A2	19910610	JP 1990-267502	19901003
	JP 04040339	B4	19920702		
	JP 03178953	A2	19910802	JP 1990-267501	19901003
	JP 05030826	B4	19930511		
PRAI	US 1982-449032	A	19821213		
	US 1983-486594	A	19830419		
	GB 1983-16646	A	19830618		
	US 1983-545701	A	19831026		
	EP 1983-307435	A	19831207		
	GB 1983-32598	A3	19831207		

OS CASREACT 102:5895; MARPAT 102:5895

GI



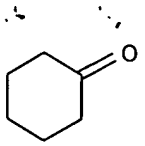
I

AB About 35 I [R1 = H, C1-6 alkyl; R2 = C1-6 alkyl; R3 = optionally unsatd. 1-hydroxycycloalkyl, optionally unsatd. 1-alkoxycycloalkyl, 1-cycloalkenyl; R4 = H, C1-6 alkyl; R5, R6 = H, OH, C1-6 alkyl, alkoxy, alkanoyloxy, -CN, NO2, alkylthio, NH2, alkylamino, dialkylamino, carboxamido, halo, CF3; R5R6 = methylenedioxy], antidepressants, were prepared E.g., p-MeOC6H4CH2CN in THF was treated with BuLi at -70°, then condensed with cyclohexanone at -50° to give 1-[cyano(p-methoxyphenyl)methyl]cyclohexanol (II). II was hydrogenated in NH3-EtOH over 5% Rh on Al2O3, then methylated with HCHO and HCO2H to give 1-[(2-dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol (III). III showed an activity equal to imipramine in synaptosomal NE and 5-HT uptake inhibition. Also, unlike the tricyclic antidepressants, III and related compds. demonstrate neither muscarinic anticholinergic activity nor antihistaminic activities.

IT **108-94-1**, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation reaction of, with lithiated phenylacetonitrile derivs.)

RN 108-94-1 CAPLUS

CN Cyclohexanone (7CI, 8CI, 9CI) (CA INDEX NAME)

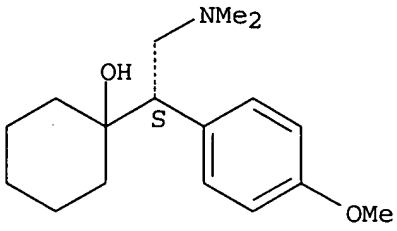


IT **93471-25-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 93471-25-1 CAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, [R-(R*,R*)]-, compd. with (S)-1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 93413-44-6
CMF C17 H27 N O2

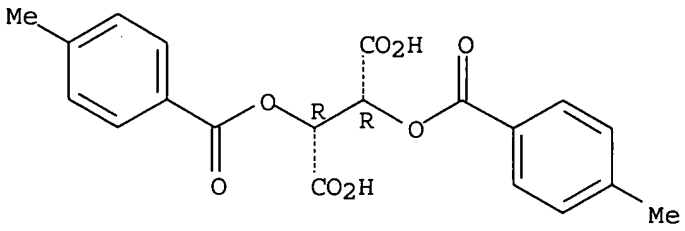
Absolute stereochemistry. Rotation (+).



CM 2

CRN 32634-66-5
CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).



L13 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:725583 CAPLUS
DN 133:296268
TI Preparation of derivatives of venlafaxine and their inhibition of neuronal monoamine reuptake
IN Jerussi, Thomas P.; Senanayake, Chrisantha H.
PA Sepracor Inc., USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000059851	A1	20001012	WO 2000-US8705	20000331
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2368083	AA	20001012	CA 2000-2368083	20000331
	EP 1165487	A1	20020102	EP 2000-920026	20000331
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003521470	T2	20030715	JP 2000-609367	20000331
	NZ 514612	A	20040130	NZ 2000-514612	20000331
	EP 1466889	A1	20041013	EP 2004-10248	20000331
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	AU 782092	B2	20050630	AU 2000-40627	20000331
	NO 2001004816	A	20011204	NO 2001-4816	20011003
	US 2004106576	A1	20040603	US 2003-720134	20031125
	US 2005197392	A1	20050908	US 2005-91518	20050329
	AU 2005218047	A1	20051027	AU 2005-218047	20050930
PRAI	US 1999-127938P	P	19990406		
	US 1999-167906P	P	19991130		
	US 2000-527442	A3	20000317		
	AU 2000-40627	A3	20000331		
	EP 2000-920026	A3	20000331		
	WO 2000-US8705	W	20000331		
	US 2003-720134	A3	20031125		

AB Preparation of derivs. of venlafaxine, e.g., O-desmethylvenlaflaxine, is described. Also disclosed are methods of treating and preventing diseases and disorders including, but not limited to, affective disorders such as depression, bipolar and manic disorders, attention deficit disorder, attention deficit disorder with hyperactivity, Parkinson's disease, epilepsy, cerebral function disorders, obesity and weight gain, incontinence, dementia and related disorders.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:384124 CAPLUS
DN 133:17270
TI Preparation of (-)-venlafaxine and derivatives as neuronal monoamine reuptake inhibitors.
IN Jerussi, Thomas P.; Senanayake, Chrisantha H.
PA Sepracor Inc., USA
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032556	A1	20000608	WO 1999-US28303	19991201
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6342533	B1	20020129	US 1999-450690	19991130
	CA 2352324	AA	20000608	CA 1999-2352324	19991201
	EP 1135359	A1	20010926	EP 1999-968056	19991201
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003524613	T2	20030819	JP 2000-585198	19991201
	AU 774408	B2	20040624	AU 2000-24749	19991201
	US 2002086904	A1	20020704	US 2001-14592	20011214
	US 6441048	B2	20020827		
	US 2003018083	A1	20030123	US 2002-222815	20020819
	US 6911479	B2	20050628		
	US 2004180952	A1	20040916	US 2004-806423	20040323
PRAI	US 1998-110488P	P	19981201		
	US 1999-450690	A	19991130		
	WO 1999-US28303	W	19991201		
	US 2001-14592	A3	20011214		
	US 2002-222815	A3	20020819		

AB A pharmaceutical composition comprising (-)-venlafaxine derivative substantially free of (+)-stereoisomer is claimed. Thus, (±)-venlafaxine in THF was added to a mixture prepared from Ph2PH and BuLi in THF at 0° followed by stirring and overnight reflux to give 73.8% (±)-O-desmethylvenlafaxine, which was resolved using di-p-toluoyl-L-tartaric acid to give (-)-O-desmethylvenlafaxine. Drug formulations containing the latter are given.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:384122 CAPLUS
DN 133:30575
TI Preparation of derivatives of (+)-venlafaxine as inhibitors of neuronal monoamine reuptake.
IN Jerussi, Thomas P.; Senannayake, Chrisantha H.
PA Sepracor Inc., USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032555	A1	20000608	WO 1999-US28306	19991201
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6197828	B1	20010306	US 1999-450691	19991130
	CA 2352321	AA	20000608	CA 1999-2352321	19991201
	EP 1135358	A1	20010926	EP 1999-965065	19991201
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2003501344	T2	20030114	JP 2000-585197	19991201
	AU 2005200129	A1	20050210	AU 2005-200129	20050112

PRAI US 1998-110486P P 19981201
US 1999-450691 A 19991130
AU 2000-31062 A3 19991201
WO 1999-US28306 W 19991201

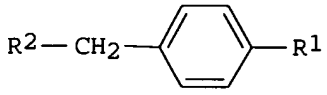
AB A method of treating an affective disorder comprises administration of a (+)-venlafaxine derivative substantially free of the (-)-enantiomer. Thus, (±)-venlafaxine (preparation given) was added to a 0° mixture of Ph2PH and BuLi followed by stirring and reflux overnight to give 73.8% (±)-O-desmethylvenlafaxine, which was resolved to give (+)-O-desmethylvenlafaxine. Drug formulations containing the latter are given.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

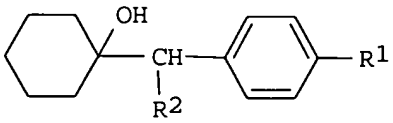
L16 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:451678 CAPLUS
DN 141:23295
TI Process for the preparation of cyclohexanol derivatives
IN Lan, Zhiyin; Shi, Kaiyun; Mo, Qizhuang; Li, Yulin
PA Peop. Rep. China
SO U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004106818	A1	20040603	US 2003-638845	20030811
	CN 1504456	A	20040616	CN 2002-153015	20021129
PRAI	CN 2002-153015	A	20021129		

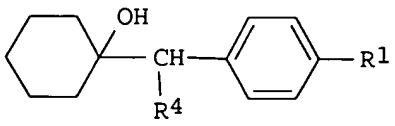
OS CASREACT 141:23295; MARPAT 141:23295
GI



I



II



III

AB A reaction of a para-substituted aryl compound I [R1 = OH, OMe; R2 = CN, CONH2, CONHMe, CONMe2] with cyclohexanone is facilitated by a metal **hydride**, such as NaH, KH, LiH, MgH2, CaH2, AlH3, and/or LiAlH4 to make first intermediates II [R1 = OH, OMe; R2 = CN, CONH2, CONHMe, CONMe2] useful in producing a drug commonly known as Venlafaxine. Alternatively, lithium diisopropylamide (diisopropylamino lithium) may be used in place of the metal **hydride**. The first intermediates II may be further reacted to form second intermediates III [R1 = OH, OMe; R4 = CH2NH2] in a reduction that is facilitated by Raney nickel or a metal **hydride**. These reaction processes may each occur in an organic solvent, which delivers highly pure reaction products in high yield. Thus, reacting p-MeOC6H4CH2CN with cyclohexanone in the presence of NaH afforded 80% II [R1 = OMe; R2 = CN]. The latter was hydrogenated over Raney Ni to give 83% III [R1 = OMe; R4 = CH2NH2].

L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:425466 CAPLUS
DN 133:17266
TI Synthesis of 1-[2-amino-1-(p-methoxybenzyl)ethyl]cyclohexanol
IN Cheng, Guohou; Zhuo, Chao
PA East China Science & Engineering Univ., Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.
CODEN: CNXXEV
DT Patent
LA Chinese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1225356	A	19990811	CN 1998-122097	19981215
PRAI	CN 1998-122097		19981215		

OS CASREACT 133:17266

AB The process comprises allowing to react 4-methoxyphenylacetonitrile with organic base at 0-5° for 0.5-2 h, adding with cyclohexanone at 0-5° for 2-4 h to obtain 1-(α-cyano-4-methoxybenzyl)cyclohexanol (I), and mixing with NaBH4 in solvent for 3-5 h, adding 40-50% BF3.etherate solution in 3-5 h, and refluxing for 1-3 h. The organic base is selected from one or more of NaOMe, NaOEt, NaNH2, and NaH. The mole ratio of 4-methoxyphenylacetronitrile-cyclohexanone- organic base is 1:1-1.3:1-1.3, and that of I-NaBH4-BF3.etherate is 1:0.9-1:1-1.12. The title compound is useful as intermediate for synthesis of the antidepressant venlafaxine.

L17 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:317433 CAPLUS
DN 144:331128
TI A process for the manufacture of venlafaxine and its intermediates
IN Gokhale, Uday Balkrishna; Parenky, Chandrashekar
PA Amoli Organics Ltd., India
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006035457	A1	20060406	WO 2005-IN314	20050916

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI IN 2004-MU997 A 20040917
AB Venlafaxine is prepared in high yield and selectivity by the drop-wise addition of a THF solution of p-methoxyphenylacetonitrile to a solution of BuLi in hexane to give 1-[cyano(4-methoxyphenyl)methyl]cyclohexanol which is then hydrogenated in toluene and water using Raney nickel as the catalyst followed by neutralization with acetic acid to give to 1-[2-amino-1-(4-methoxyphenyl)ethylcyclohexanol] acetate which is then dimethylated with formaldehyde and neutralized with HCl to give venlafaxine hydrochloride.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:141623 CAPLUS
DN 144:331066
TI Method of preparation venlafaxine and its salts as antidepressant
IN Zhao, Zhiquan
PA Lunan Pharmaceutical Co., Ltd., Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1640867	A	20050720	CN 2004-10002726	20040119
PRAI CN 2004-10002726		20040119		

OS CASREACT 144:331066
AB The method comprises condensing p-methoxybenzyl cyanide with cyclohexanone in the presence of base (such as KOH, NaOH, Ca(OH)2, sodium methoxide) in hexane (or benzene, THF, ether) at -10 to +25°C for 6-26 h to give condensation product; then reducing with Raney Ni (or Red-Al) in methanol (or ethanol, Et acetate, acetic acid) at 10-45°C for 4-24 h to give amine; at last methylating amine with formaldehyde and formic acid (or Me iodide, Me bromide) to give venlafaxine; and/or reacting with HCl, HBr, HI, HNO3, H2SO4, citric acid, maleic acid, tartaric acid to give venlafaxine salt. The venlafaxine and its salts can be used as antidepressant.

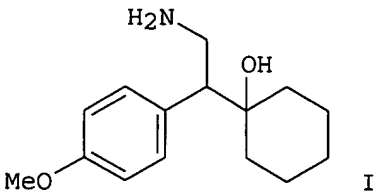
L17 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:6307 CAPLUS

TI Synthesis and molecular structure analysis of venlafaxine intermediate and its analog
AU Kavitha, C. V.; Lakshmi, S.; Basappa; Mantelingu, K.; Sridhar, M. A.; Prasad, J. Shashidhara; Rangappa, K. S.
CS Department of Studies in Chemistry, University of Mysore, Mysore, 570006, India
SO Journal of Chemical Crystallography (2005), 35(12), 957-963
CODEN: JCCYEV; ISSN: 1074-1542
PB Springer
DT Journal
LA English
AB 1-(cyano-(4-methoxyphenyl)methyl)cyclohexanol, a Venlafaxine intermediate was crystallize in both monoclinic (I) and orthorhombic (II) crystal systems. The form I crystallizes in the space group C2/c with the cell parameters a = 23.506(3), b = 5.550(3), c = 23.192(3), and β = 115.116(2)°. The form II crystallizes in space group P212121 with cell parameters a = 5.7850(6), b = 11.2680(6), c = 20.6730(19). The intermol. hydrogen bonding in the case of the monoclinic polymorph leads to the formation of dimer. The synthesis, characterization, and crystal structure studies of Venlafaxine analog 1-[2-1-(4-dimethylamino-phenyl)-ethylideneamino-1-(4-methoxy-phenyl)-ethyl]-cyclohexanol (III) is reported. The compound III crystallizes in P.hivin.1 space group with cell parameters a = 10.801(7), b = 12.078(7), c = 9.928(5), α = 96.12(5)% , β = 110.49(5)°, γ = 112.42(6)°.
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:602707 CAPLUS
DN 143:193736
TI Venlafaxine intermediate
AU Anon.
CS USA
SO IP.com Journal (2005), 5(2), 34 (No. IPCOM000035604D), 26 Jan 2005
CODEN: IJPOBX; ISSN: 1533-0001
PB IP.com, Inc.
DT Journal; Patent
LA English

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI IP 35604D		20050126		
PRAI IP 2005-35604D	20050126			

GI



I

AB A method to prepared the venlafaxine intermediate, 1-[2-amino-1-(4-methoxyphenyl)ethyl]cyclohexanol (I), is described. 4-Methoxyphenylacetonitrile is added to cyclohexanone to produce 1-[cyano(4-methoxyphenyl)methyl]cyclohexanol which is subsequently reduced to provide I.

L17 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:529114 CAPLUS
DN 144:275964
TI Synthesis of Venlafaxine Hydrochloride
AU Zhao, Zhiquan; Peng, Lizeng
CS Lunan Pharmaceutical Co. Ltd., Linyi, Shandong Province, 276003, Peop. Rep. China

SO Zhongguo Yiyao Gongye Zazhi (2004), 35(10), 577-578
CODEN: ZYGZEA; ISSN: 1001-8255
PB Zhongguo Yiyao Gongye Zazhi Bianjibu
DT Journal
LA Chinese
OS CASREACT 144:275964
AB Venlafaxine hydrochloride was synthesized by condensation of 4-methoxybenzyl cyanide with cyclohexanone in presence of KH in toluene to give α-(1-hydroxycyclohexyl)-4-methoxybenzyl cyanide, which subjected to reduction by Red-Al or NiCl2/NaBH4 and subsequent methylation. The overall yield of venlafaxine hydrochloride was 50%-62%.

L17 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:123222 CAPLUS
DN 142:197679
TI Hydrogenation process for the preparation of 1-[2-amino-1-(4-methoxyphenyl)ethyl]cyclohexanol which is an intermediate of venlafaxine hydrochloride
IN Reguri, Buchi Reddy; Kadaboina, Rajasekhar; Gade, Srinivas Reddy; Ireni, Babu
PA Reddy's Laboratories Limited, India; Reddy's Laboratories, Inc.
SO U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005033088	A1	20050210	US 2004-862890	20040607
PRAI IN 2003-MA460	A	20030606		

OS CASREACT 142:197679
AB 1-[2-Amino-1-(4-methoxyphenyl)ethyl]cyclohexanol (I) is prepared by the hydrogenation of 1-[cyano(4-methoxyphenyl)methyl]cyclohexanol in the presence of a heterogeneous Pd/C catalyst. I is converted into venlafaxine hydrochloride by N-methylylation with formaldehyde followed by neutralization of the free base with HCl.

L17 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:948896 CAPLUS
DN 142:176464
TI Method for continuous preparation of venlafaxine intermediate
IN Jung, Gi Nam; Kim, Myeong Rae; Ko, Gi Ho; Kwak, Byeong Seong; Lee, Sang Su
PA SK Corporation, S. Korea
SO Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DT Patent
LA Korean
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI KR 2003065889	A	20030809	KR 2002-5944	20020201
PRAI KR 2002-5944		20020201		

AB Provided is a method for relatively simply, economically and efficiently producing amino methoxy Ph Et cyclohexanol which is a venlafaxine intermediate, in high yield. The method comprises the steps of (i) reacting 0.8-1.2 mol of methoxy Ph acetonitrile with 0.8-1.2 mol of Grignard reagent(RMgX, wherein R is C1-C10 alkyl group, X is halogen) at -10 to 5° in the presence of solvent, and further reacting the reaction product with 1 mol of cyclohexanone to obtain cyano methoxy Ph Et cyclohexanol; and (ii) hydrogenating the cyano methoxy Ph Et cyclohexanol at a temperature of 0-200°, under the pressure of 10-200 bar, and at weight hourly space velocity(WHSV) of 0.1-15 h-1 in the presence of catalyst system formed by supporting hydrocarbon solvent, basic additives and metal on a carrier.

L17 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:729755 CAPLUS
DN 141:379671

TI An efficient and green protocol for the preparation of cycloalkanols: a practical synthesis of venlafaxine

AU Chavan, Subhash P.; Khobragade, Dushant A.; Kamat, Subhash K.; Sivadasan, Latha; Balakrishnan, Kamalam; Ravindranathan, T.; Gurjar, Mukund K.; Kalkote, Uttam R.

CS Division of Organic Chemistry: Technology, National Chemical Laboratory, Pune, 411008, India

SO Tetrahedron Letters (2004), 45(39), 7291-7295
CODEN: TELEAY; ISSN: 0040-4039

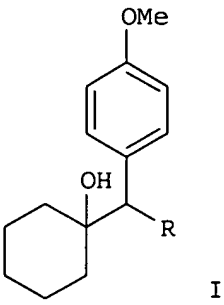
PB Elsevier B.V.

DT Journal

LA English

OS CASREACT 141:379671

GI

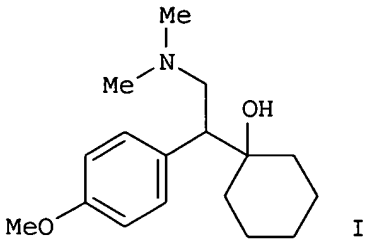


I

AB The condensation of arylacetonitriles with cyclic ketones using aqueous NaOH or KOH under phase transfer catalysis gave almost quant. yields of benzylcycloalkanols, e.g., I (R = CN). This protocol was utilized for a practical synthesis of the antidepression drug, venlafaxine I (R = NMe2).

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:403889 CAPLUS
DN 141:140121
TI Simple and an efficient method for the synthesis of 1-[2-dimethylamino-1-(4-methoxyphenyl)-ethyl]-cyclohexanol hydrochloride: (±) venlafaxine racemic mixtures
AU Basappa; Kavitha, C. V.; Rangappa, K. S.
CS Department of Studies in Chemistry, University of Mysore, Mysore, 570006, India
SO Bioorganic & Medicinal Chemistry Letters (2004), 14(12), 3279-3281
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science B.V.
DT Journal
LA English
OS CASREACT 141:140121
GI



I

AB A synthetic method has been developed for the synthesis of venlafaxine (I) using inexpensive reagents. This method is an improvement on previous methods, a simple and efficient method for the large-scale synthesis of venlafaxine.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:472478 CAPLUS
DN 139:41833
TI Preparation of venlafaxine hydrochloride crystalline polymorphs
IN Rameshchandra, Sonak Bhavin; Patel, Mahesh Shankarbhai; Patel, Gaurang Balkrushna; Ramakrishna, Nirogi Venkata Satya; Manakiwala, Satish Champaklal; Agarwal, Virendra Kumar; Pandita, Kanwal; Patel, Pankaj Ramanbhai
PA Cadila Healthcare Limited, India
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003050074	A1	20030619	WO 2002-IN46	20020319
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002247945	A1	20030623	AU 2002-247945	20020319
PRAI IN 2001-MU1177	A	20011213		
WO 2002-IN46	W	20020319		

AB The present invention discloses process for the preparation of venlafaxine-HCl

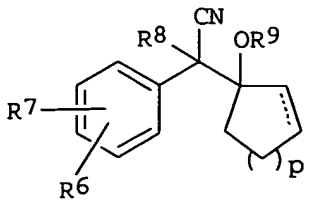
(I) and its novel crystalline polymorphs designated as Form I, Form II, Form III and crystalline forms of (R)- and (S)- enantiomers. These are characterized by specific FT-IR, x-ray powder diffraction and Solid-state NMR (13C-CP/MAS NMR) and are useful as agents for treating depression. Thus, I was prepared by the reaction of p-methoxyphenylacetonitrile with cyclohexanone in the presence of NaOH in a mixture of toluene and hexane, followed by the hydrogenation over Raney Nickel in the presence of anhydrous NH3, methylation with HCHO and HCO2H, and finally treatment with anhydrous HCl.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

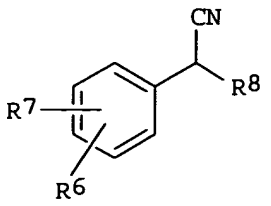
L17 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:5924 CAPLUS
DN 138:73016
TI Improved process for preparation of cyclohexanol derivatives, e.g., 1-[cyano(4-methoxyphenyl)methyl]cyclohexanol, a venlafaxine intermediate, from phenylacetonitriles and cyclohexanone, using non-organometallic bases.
IN Kim, Keun-sik; Kim, Kwang-il; Lee, Sung-woo; Park, Jin-soo; Chai, Ki-byung
PA Wyeth A Corporation of the State of Delaware, USA, USA
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003000652	A1	20030103	WO 2002-US19753	20020621
	WO 2003000652	C1	20040521		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2450914	AA	20030103	CA 2002-2450914	20020621
	EP 1397344	A1	20040317	EP 2002-744526	20020621
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2002010542	A	20040622	BR 2002-10542	20020621
	CN 1531524	A	20040922	CN 2002-812466	20020621
	JP 2004531577	T2	20041014	JP 2003-507059	20020621
	US 2004186310	A1	20040923	US 2003-481679	20031219
	ZA 2004000451	A	20050421	ZA 2004-451	20040121
PRAI	KR 2001-35889	A	20010622		
	WO 2002-US19753	W	20020621		

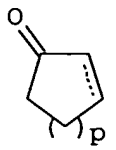
OS CASREACT 138:73016; MARPAT 138:73016
GI



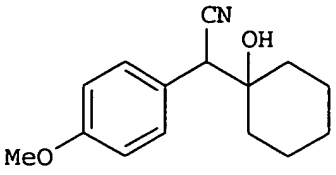
I



II



III



IV

AB An improved process for the preparation of cyanobenzylated cyclohexanol derivs. and analogs I is claimed [wherein: R6 and R7 are ortho or para substituents, independently selected from the group consisting of H, OH, C1-C6 alkyl, C1-C6 alkoxy, C7-C9 aralkoxy, C2-C7 alkanoyloxy, C1-C6 alkylmercapto (sic), halo, or CF3; R8 is H or C1-C6 alkyl; p is 0, 1, 2, 3 or 4; and R9 is H or C1-C6 alkyl]. Reaction of phenylacetonitriles II with cycloalk(an/en)ones III in the presence of a non-organometallic base catalyst IV or V, in the presence or absence of a reaction solvent, gives I [wherein: A is (CH2)n where n is 2 to 4; B is (CH2)m where m is 2 to 5; X is CH2, O, NH or NR', where R' is C1-C4 alkyl or acyl, or an alkyl supporting polymer; and each of R1 to R4 is independently H, alkyl, cycloalkyl, or an alkyl or cycloalkyl supporting polymer, and all of R1 to R4 are not H; R5 is alkyl, cycloalkyl, or an alkyl or cycloalkyl supporting polymer; and where R9 is an alkyl, the alkyl group is introduced by alkylation]. The products, such as IV, are useful intermediates for antidepressants such as venlafaxine. Known methods relying upon organometallic bases such as n-BuLi are expensive, at risk of fire or explosion, give low yields, and are impractical on an industrial scale. In contrast, the invention method is simple, economical, scalable to industrial production, safe, and environmentally friendly. Only small, catalytic amts. of the base are needed, and use of organic solvents is avoided. Both yields and purity of products are high. For instance, solventless reaction of 0.68 mol p-methoxyphenylacetonitrile with 1.02 mol cyclohexanone in the presence of 0.21 mol DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) for 48 h at 15-20°, followed by addition of 1N HCl to acid pH and stirring for 1 h at room temperature, gave IV in 84% yield by simple precipitation and filtration, m. 123.7°. The same procedure with only 0.1 equiv DBU and a reaction time of 6 days gave 90.5% yield. In contrast, a standard, more complex preparation of using n-BuLi in THF gave only 34.2% yield of lower-purity IV. Another preparation using LDA (from n-BuLi and diisopropylamine) gave 79% yield of IV, but required a large amount of toluene as solvent.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:792121 CAPLUS
DN 137:294862
TI Preparation of the key epoxide intermediate for the production of 1-[2-dimethylamino-1-(4-methoxyphenyl)ethyl]cyclohexanol
IN Rathod, Dhiraj Mohansinh; Rengaraju, Srinivasan; Gharpure, Milind Moreshwar; Patel, Nishant Mahendra; Deoahar, Mandar Manohar
PA Alembic Limited, India
SO Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

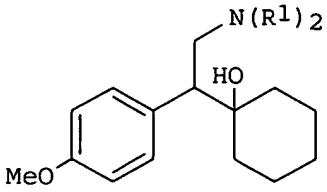
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1249447	A1	20021016	EP 2001-303347	20010410

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

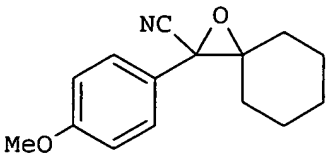
	CA 2381334	AA	20021010	CA 2002-2381334	20020409
	US 2003195376	A1	20031016	US 2002-119287	20020410
	US 6756502	B2	20040629		
PRAI	EP 2001-303347	A	20010410		

OS CASREACT 137:294862

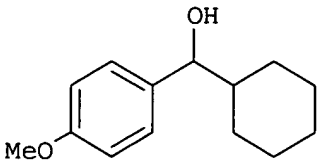
GI



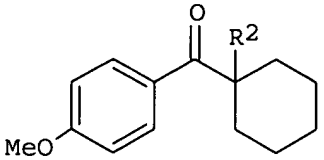
I



II



III



IV

AB Processes for the preparation of venlafaxine (I; R1 = Me) via the novel epoxy-nitrile intermediate II, which when subjected to hydrogenation forms precursor I (R1 = H) and may subsequently be reductively methylated to the desired I (R1 = Me); II itself may be synthesized via various alternative reaction strategies, from a range of starting materials. Thus, 4-MeOC6H4CHO, upon treatment with cyclohexylmagnesium bromide, yields carbinol III; III may then be oxidized to ketone IV (R2 = H), which forms bromide IV (R2 = Br) on treatment with an α-keto halogenating agent; cyanation of the later, then yields the desired II, from which I (R = Me) may be synthesized.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2002:658793 CAPLUS

DN 137:185318

TI Process for the preparation of 1-[cyano(aryl)methyl]cyclohexanols by the aldol condensation of phenylacetonitriles with cyclohexanone

IN Chavan, Subhash Prataprao; Kamat, Subhash Krishnaji; Sivadasan, Latha; Balakrishnan, Kamalam; Khobragade, Dushant Anandrao; Thottapillil, Ravindranathan; Gurjar, Mukund Keshao; Kalkote, Uttam Ramrao

PA Council of Scientific and Industrial Research, India

SO U.S. Pat. Appl. Publ., 4 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

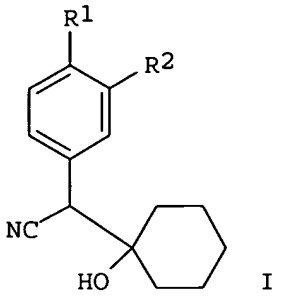
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002120164	A1	20020829	US 2001-796084	20010228
	US 6504044	B2	20030107		
	EP 1238967	A1	20020911	EP 2001-301840	20010228
	EP 1238967	B1	20050427		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

	AT 294157	E	20050515	AT 2001-301840	20010228
PRAI	EP 2001-301840	A	20010228		
	US 2001-796084	A	20010228		

OS CASREACT 137:185318

GI



I

AB The invention relates to a process for the preparation of 1-[(cyano)arylmethyl]cyclohexanols [I; (a) R1 = H, R2 = H; (b) R1 = OMe, R2 = H; (c) R1 = OMe, R2 = OMe; (d) R1 = OMe, R2 = cyclopentyloxy; e.g., 2-(1-hydroxycyclohexyl)-2-phenylacetonitrile] in high yield and selectivity by the aldol reaction of cyclohexanone with the carbanions of a correspondingly substituted phenylacetonitrile (e.g., phenylacetonitrile) in the presence of a catalytic quantity of a base (e.g., sodium hydroxide) at 0-15° for 15-120 min, and isolating and purifying the I compound by crystallization More particularly the invention relates to the preparation of 1-[cyano(4-methoxyphenyl)methyl]cyclohexanol [I; R1 = OMe, R2 = H], a key intermediate for the synthesis of Venlafaxine.

L17 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:449634 CAPLUS
DN 137:20211
TI Novel crystalline polymorphic forms of venlafaxine hydrochloride and a process for their preparation
IN Siripragada, Mahender Rao; Krishnamurthi, Vyas; Arikatla, Siva Lakshmi Devi; Gaddam, Om Reddy
PA Reddy's Research Foundation, India
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002046140	A1	20020613	WO 2000-IN121	20001207
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001035970	A5	20020618	AU 2001-35970	20001207
PRAI	WO 2000-IN121	A	20001207		

OS CASREACT 137:20211

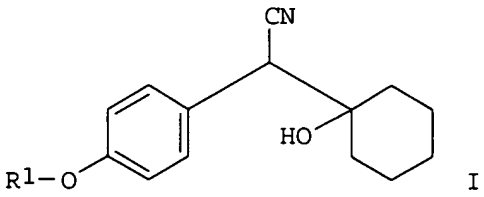
AB Novel crystalline polymorphic forms of venlafaxine hydrochloride are prepared by heating and cooling solvents containing the title compound; DSC, X-ray, and IR spectral data of the different polymorphs is presented.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:171843 CAPLUS
DN 136:216536
TI Process for the preparation of substituted phenylacetonitriles via the aldol reaction of cyclohexanone with phenylacetonitriles in the presence of a base
IN Ekkundi, Vadiraj S.; Mumbaikar, Vilas N.; Paingankar, Niranjan; Van Der Schaaf, Paul Adriaan
PA Ciba Specialty Chemicals Holding Inc., Switz.
SO PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002018325	A2	20020307	WO 2001-EP9665	20010821
	WO 2002018325	A3	20030109		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2418040	AA	20020307	CA 2001-2418040	20010821
	AU 2001091785	A5	20020313	AU 2001-91785	20010821
	EP 1313698	A2	20030528	EP 2001-971945	20010821
	EP 1313698	B1	20041103		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004507520	T2	20040311	JP 2002-523443	20010821
	AT 281429	E	20041115	AT 2001-971945	20010821
	TR 200300251	T2	20041221	TR 2003-200300251	20010821
	CN 1608049	A	20050420	CN 2001-814805	20010821
	US 2003139623	A1	20030724	US 2002-130010	20021001
	US 6620960	B2	20030916		
PRAI	IN 2000-MA705	A	20000830		
	WO 2001-EP9665	W	20010821		

OS CASREACT 136:216536; MARPAT 136:216536
GI



I

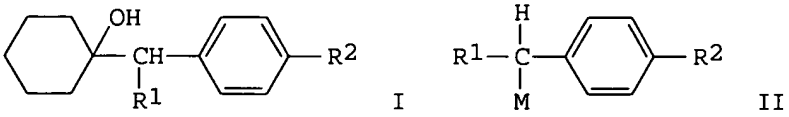
AB Phenylacetonitriles [I; R1 = (un)substituted alkyl; e.g., R1 = Me] are prepared by the aldol condensation of phenylacetonitriles 4-R1OC6H4CH2CN (e.g., 4-methoxyphenylacetonitrile) with cyclohexanone in the presence of an aqueous base (e.g., aqueous NaOH) and a phase-transfer catalyst (e.g., tetrabutylammonium chloride).

L17 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:621161 CAPLUS
DN 132:107716
TI Studies on synthesis of antidepressant venlafaxine
AU Zhou, Jinpei; Zhang, Huibin; Huang, Xuezhen; Huang, Wenlong
CS Division of Medicinal Chemistry, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SO Zhongguo Yaoke Daxue Xuebao (1999), 30(4), 249-250
CODEN: ZHYXE9; ISSN: 1000-5048
PB Zhongguo Yaoke Daxue
DT Journal
LA Chinese
AB The title antidepressant venlafaxine, a noradrenalin and 5-HT uptake inhibitor (SSRIs) with fewer side effects than tricyclic antidepressant drugs, was prepared with 11% yield in five steps from methoxybenzene in moderate condition suitable for a scale-up production

L17 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:81228 CAPLUS
DN 114:81228
TI Preparation of cyclohexanol derivatives as intermediates for antidepressants
IN Shepherd, Robin Gerald
PA John Wyeth and Brother Ltd., UK
SO Brit. UK Pat. Appl., 15 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

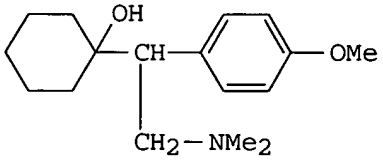
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2227743	A1	19900808	GB 1990-2095	19900130
	GB 2227743	B2	19920617		
	US 5043466	A	19910827	US 1990-471187	19900126
PRAI	GB 1989-2209	A	19890201		

OS CASREACT 114:81228; MARPAT 114:81228
GI



I

II



III

AB Title compds. I [R1 = cyano, CONMe2, CSNMe2; R2 = OMe, (protected) OH], useful as intermediates for preparation of antidepressants, were prepared by reaction of II [M = Li, Na, K, or MgX (X = halo); R2 = OMe, protected OH] with cyclohexanone in hydrocarbon/ether solvents. For example, II (R1 = CSNMe2, R2 = OMe, M = MgBr) gave the corresponding I in 64% yield. Subsequent reduction of I by Raney-Ni gave the antidepressant (no data) N,N-dimethyl-2-(1-hydroxycyclohexyl)-2-(4-methoxyphenyl)ethylamine (III).

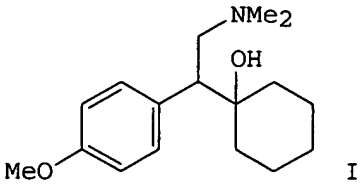
L17 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1990:630878 CAPLUS
DN 113:230878
TI 2-Phenyl-2-(1-hydroxycycloalkyl)ethylamine derivatives: synthesis and

antidepressant activity

AU Yardley, John P.; Husbands, G. E. Morris; Stack, Gary; Butch, Jacqueline; Bicksler, James; Moyer, John A.; Muth, Eric A.; Andree, Terrance; Fletcher, Horace, III; et al.
CS Wyeth-Ayerst Res., Princeton, NJ, 08543-8000, USA

SO Journal of Medicinal Chemistry (1990), 33(10), 2899-905
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CASREACT 113:230878

GI



I

AB A series of 2-phenyl-1-(1-hydroxycycloalkyl)ethylamine derivs. was examined for the ability to inhibit both rat brain imipramine receptor binding and the synaptosomal uptake of norepinephrine (NE) and serotonin (5-HT). Neurotransmitter uptake inhibition was highest for a subset of 2-phenyl-2-(1-hydroxycyclohexyl)dimethylethylamines in which the aryl ring has a halogen or methoxy substituent at the 3- and/or 4-positions. Potential antidepressant activity in this subset was assayed in three rodent models-the antagonism of reserpine-induced hypothermia, the antagonism of histamine-induced ACTH release, and the ability to reduce noradrenergic responsiveness in the rat pineal gland. An acute effect seen in the rat pineal gland with several analogs, including 1-[1-(3,4-dichlorophenyl)-2-(dimethylamino)ethyl]cyclohexanol and 1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol (I), was taken as a possible correlate of a rapid onset of antidepressant activity. Compound I (venlafaxine) is presently undergoing clin. evaluation.